DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

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NADA 140-929

Melissa Veenhuizen, DVM, MS, Dipl. ABVP
Elanco Regulatory Affairs, Manager Surveillance & Compliance
Elanco Animal Health
2001 W. Main Street, DC G1.21
Greenfield, IN 46140

Re: NADA 140-929
Micotil® 300 (Tilmicosin phosphate) Tilmicosin injection, USP—Promotional pieces coded: AI9615 (6/04); AI9613 (5/04); AI9622 (7/04).

Dear Dr. Veenhuizen:

The Division of Surveillance (DOS) has reviewed a promotional piece entitled Tech Report, Research Information for the Veterinarian from Elanco Animal Health, "The Use of Micotil® Metaphylaxis for the Control of Undifferentiated Bovine Respiratory Disease: A 28-Trial Summary" [AI9615 (6/04)] for Micotil® 300 (Tilmicosin phosphate) Tilmicosin injection, USP submitted by Elanco Animal Health under cover of form FDA 2301 dated June 23, 2004. Additional promotional pieces include two brochures [AI9613 (5/04) and AI9622 (7/04)] submitted by Elanco Animal Health under cover of form FDA 2301 dated June 07, 2004. The materials are misleading because they contain unsubstantiated efficacy claims, causing the drug to be misbranded under Section 502(a) of the Federal Food, Drug, and Cosmetic Act.

Background

Indications: Micotil 300 is indicated for the treatment of bovine respiratory disease (BRD) and ovine respiratory disease (ORD) associated with *Mannheimia (Pasteurella) haemolytica*. Micotil 300 is also indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia (Pasteurella) haemolytica*.

Unsubstantiated Effectiveness Claims

The Tech Report and two brochures claim that metaphylactic use of Micotil 300 in cattle reduces morbidity by 49.2%, reduces mortality by 68.2% and improves daily gain by 8.5%. These percentages are based on pooled data from a "28-Trial Summary." The "28-Trial Summary" uses 28 dissimilar studies to generate the percentages on which to base the efficacy claims. The brochures present these same efficacy claims in the form of bar graphs based on the percentages presented in the Tech Report.

Using percentages to quantify claims for reduction in morbidity and mortality and for improved daily gain suggests that there is an objective measure for determining the effectiveness of this drug; such effectiveness claims must be based on substantial evidence or substantial clinical experience. The "28-Trial Summary," which is based on pooled data from 28 dissimilar studies, is not substantial evidence or substantial clinical experience for the following reasons.

The studies vary in duration from 21 to 250 days. This much variation in trial duration means the treatment groups in each of the trials vary greatly in age. It also means that some studies involved seasonal changes while others did not. References indicate that the studies were performed in several states, and in at least two countries. Thus, the animals in the studies were exposed to different climates and conditions. The earliest studies were published in 1990 and the most recent in 2003, indicating that the studies may have been performed over a period of 13 years. This fact is significant because during this time period, cattle have changed genetically and cattle feeding, management, and husbandry practices have changed. It also appears that there were differences in the number of cattle used in each study.

Finally, the percentages for reduced mortality, reduced morbidity, and improved daily gain are apparently determined by averaging the results from each study. Averaging results assigns equal statistical power to each of the studies. However, the studies are not of equal statistical power because, as described above, they differ in duration and numbers of cattle in the treatment groups.

CVM is not aware of substantial evidence or substantial clinical experience to support the morbidity, mortality, and weight gain claims made in these promotional pieces.

Conclusion and Requested Action

DOS requests that Elanco Animal Health immediately cease the dissemination of the above described promotional pieces for Micotil® 300 and any other materials containing similar information. Please submit a written response to this letter within 30 days of its receipt describing your intent to comply with this request and explaining your plan for discontinuing use of such materials. Please direct your response to me at the Food and Drug Administration, Division of Surveillance, HFV-216, 7519 Standish Place, Rockville, MD 20855. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Micotil® 300 comply with the requirements of the Act and FDA implementing regulations.

Sincerely yours,

Mohammad I. Sharar, DVM., M.Sc.
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